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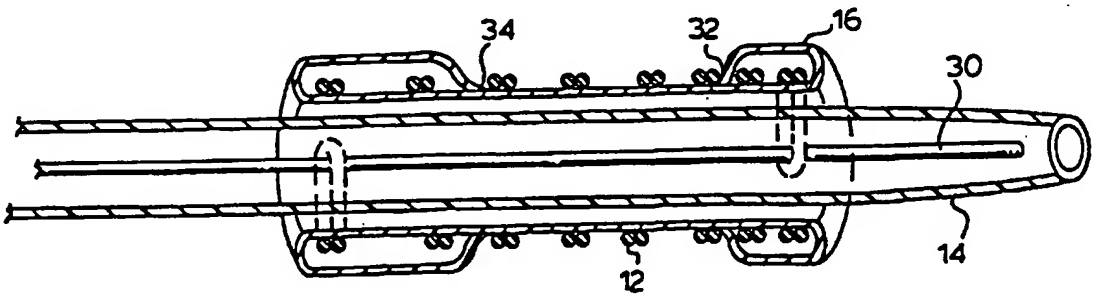

(57) Abstract

A stent having an inner tubular lining of a biomaterial. The inner lining has open ends which may be rolled about the ends of the stent. The ends of the tube are then attached to the tube itself. Alternatively, the inner tube lining is attached directly to the stent. A method of covering a stent includes mounting a tube of biomaterial on a distal end of a catheter and mounting the stent over the biomaterial. The biomaterial may be seeded with endothelial cells.

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METHOD OF COVERING A STENT WITH ACELLULAR MATRIX

FIELD OF INVENTION

This invention relates to a method of covering a stent with biomaterial. In particular, this invention relates to a method of covering a stent with acellular matrix.

BACKGROUND OF INVENTION

Stents, consisting of an "open" metal scaffolding, are now widely used for supporting narrowed or stenotic blood vessels that have been opened or expanded by balloon angioplasty. The stent is deployed to its target location within a vessel by threading the stent-carrying catheter through the vessel from an incision or percutaneous puncture some distance away. The stent is then expanded either on its own accord or by ballooning the catheter for supportive engagement with the interior of the vessel wall to maintain vessel enlargement.

Balloon expandable stents are typically metal mesh that are mounted on balloon catheters and delivered to the target location. When the balloon is expanded, the stent expands to the desired diameter to support the interior of the vessel. Examples of such stents are described in United States Patent Nos.: 5,059,211; 5,282,824; 5,306,286; and 5,334,201.

Self-expanding stents are made of an alloy having a "memory" that expand to the desired size after being placed at the target site of the vessel. Examples of such stents are described in United States Patent Nos.: 4,800,882; 5,282,824; and 5,342,387.

In United States Patent No. 5,342,387, Summers, a wire double helix stent design is illustrated. The double helix is advantageous because by narrowing and widening the gaps between the parallel struts, it can be contracted and expanded in diameter without changing its length.

Although balloon expandable stents of the prior art have been very successful in treating narrowed or occluded blood vessels, these stents still suffer from a serious drawback.

All intravascular stents consist of an open metal scaffolding. The ratio of open space to stent material varies from 80/20 to about 90/10. When the vessel is stretched by balloon angioplasty and a stent is expanded in place across a now dilated lesion, a healing response is triggered. The healing response is a proliferation of smooth muscles cells from the area of vessel wall which has been injured by the procedure. Although the scaffolding effect of the stent serves to restrict the build up of scar tissue (smooth muscle cell proliferation) and subsequent renarrowing, the gaps in the metal provide an opportunity for ensuing smooth muscle cell proliferation to grow through the open spaces of the stent. As a result, about 30% of patients will experience restenosis of the vessel. The stent and the expansion of the vessel initiates a reaction which causes tissue ingrowth (intimal hyperplasia) which eventually leads to renarrowing or restenosis, which may necessitate a revascularization procedure to reopen the narrowed area inside the stent. This additional intervention is costly and, more importantly, exposes the patient to further risk.

Attempts have been made to minimize these complications. In United States Patent No. 5,282,824, Gianturco, a stent assembly is disclosed which has a flexible nylon sleeve attached to the outside circumferential surface of a stent. On implantation of the stent, the sleeved stent is allowed to expand, pressing the flexible sleeve against the walls of the blood vessel. The sleeve is intended to prevent tissue growth between the gaps defined by the stent. However, nylon and other synthetic materials probably will not provide a long term solution as such materials can cause massive inflammatory or thrombogenic reactions.

Recently, investigators have developed materials which are not associated with thrombosis or inflammatory reactions. Acellular matrix is a biomaterial derived from tissue extracted from mammalians which is processed to remove all cells and soluble proteins. This biomaterial has been shown to be non-thrombogenic and non-inflammatory. Acellular matrix comprises a framework of largely insoluble collagen and elastin, which are very stable proteins. Experimental studies with this matrix have been successful in a variety of cardiovascular applications. (Courtman et al.: "Development of Pericardial Acellular Matrix Biomaterial: Biochemical and Mechanical Effects of Cell Extraction" Journal of Biomedical Materials Research, Vol. 28, 655-666 (1994), and Wilson et al. "Acellular Matrix Allograft Small Caliber Vascular Protheses", Vol. XXXVI Trans. AM. Soc. Artif. Intern Organs, (1990), and see also United States Patent nos. 4,776,853 and 4,801,299)

Heretofore, acellular matrices have been surgically implanted during experimental studies. Acellular matrix prothesis have not been incorporated as an integral part of stents.

In addition, investigations have also been undertaken into the effects of endothelial seeding on damaged vascular surfaces after angioplasty has exposed the subendothelial layer and caused intimal dissection of the vessel. Furthermore, animal studies have demonstrated that rapid restoration of an endothelial cell monolayer significantly reduces subsequent platelet deposition and may reduce the rate of actute arterial reocclusion. (Thompson et al.: "Platelet deposition after angioplasty is abolished by restoration of the endothelial cell monolayer" Journal of Vascular Surgery, Vol. 19. No. 3 (1994); Bearn et al.: "Prosthetic Graft Seeding: Breathing New Life into Old Grafts" J.R. Cell Surg. Edinb 39, February, 1994)

Summary of the Invention

The disadvantages of the prior art may be overcome by providing a stent with a biomaterial covering for implantation, wherein the stent is prepared by inserting biomaterial through the stent when the stent. The combined biomaterial and stent is capable of being transluminally or surgically inserted to a target site.

It is desirable to provide an acellular matrix or other biomaterial covering for a stent, wherein the covering is non-thrombogenic and inhibits tissue ingrowth when deployed inside a blood vessel, duct, or conduit.

It is further desirable to provide a stent with an acellular matrix or other biomaterial covering, wherein the biomaterial is seeded with endothelial cells.

It is desirable to provide an acellular matrix or other biomaterial covering which can form a barrier between an implanted stent and the wall of the host blood vessel, duct, or conduit.

It is further desirable to provide an acellular matrix or other biomaterial covering which provides a smooth inner surface through which fluid flows.

It is further desirable to provide an acellular matrix or other biomaterial covering to encourage organized growth from the anastomosis sites inward.

It is further desirable to provide a plurality of stents covered with an acellular matrix or other biomaterial on a single catheter for multiple deployment of the stents.

It is still further desirable to provide a stent covered with an acellular matrix or other biomaterial for use as a vascular graft for bypassing stenotic or occluded blood vessels.

It is still further desirable to provide a stent covered with acellular matrix or other

biomaterial for use as a stent or graft for other ducts or conduits within a living body.

It is still further desirable to provide a stent lined with acellular matrix or other biomaterial that restricts tissue ingrowth for congenital vascular defects such as pulmonary artery stenosis, portacaval shunts, arterio-venous shunts, deterioration of saphenous vein grafts for coronary artery by-pass grafts and peripheral arteries and endoluminal grafting.

According to one aspect of the invention, a method of preparing a stent for implantation is provided wherein an open ended tube of biomaterial is placed relatively inside the stent.

According to another aspect of the invention, the use of a stent with biomaterial for treating occlusion and stenosis of a blood vessel is provided, wherein the use comprises the steps of: providing a catheter having a distal end; mounting acellular matrix or other biomaterial on the distal end of the catheter; sliding a stent over the biomaterial; attaching the biomaterial to the stent; delivering the stent and biomaterial to a target site; expanding the stent; and withdrawing the catheter. The biomaterial is attached to the stent by suturing, surgically stapling, taping, gluing or other suitable means.

In another aspect of the invention, the distal and proximal ends of the biomaterial are rolled back over the ends of the stent and the tube ends are attached to the tube itself or the ends are attached together. The biomaterial is attached to itself by suturing, surgically stapling, taping, gluing or other suitable means.

In another aspect of the invention, the acellular matrix or other biomaterial is seeded with endothelial cells. The biomaterial may be seeded before or after it is placed on the stent. Alternatively, the biomaterial may be seeded *in situ* once the stent and biomaterial are implanted.

In another aspect of the invention, the stent and biomaterial is covered by a protective sheath and delivered to a target site and expanded by removing the protective sheath.

According to another aspect of the invention, the use of a stent with biomaterial for treating occlusion and stenosis of a blood vessel is provided. The use comprises the steps of: providing a catheter having a distal end and an internal release wire; mounting a tubular acellular matrix on the distal end of the catheter; sliding a self-expanding stent over the matrix, the self-expanding stent having a protective sheath; extending the distal and proximal ends of the stent through the acellular matrix to engage the release wire, contracting the stent into an implantable condition; withdrawing the sheath; rolling, respectively, the distal and proximal ends of the tubular acellular matrix over the distal and proximal ends of the stent; attaching the distal and proximal ends of the tubular acellular matrix to the matrix, inserting the catheter distal end into the blood vessel; guiding the catheter distal end to a targeted portion of the blood vessel; withdrawing the release wire, allowing the stent to expand; and withdrawing the catheter from the blood vessel. The distal and proximal ends of the tubular acellular matrix may be attached together.

According to another aspect of the invention, a stent with a covering of acellular matrix or other biomaterial is provided. The acellular matrix or other biomaterial is attached to the stent by suturing, surgical stapling, gluing, taping or other suitable means for attaching the biomaterial to the stent. The biomaterial may be seeded with endothelial cells.

According to another aspect of the invention, a stent with an inner tubular lining of acellular matrix or other biomaterial is provided. The inner lining has open ends for

rolling about ends of the stent. The open ends of the inner tubular lining are attached to the tube or to each other. The acellular matrix may be seeded with endothelial cells.

Description of the Drawings

In drawings which illustrate embodiments of the invention:

Figure 1 is a perspective view of an embodiment of the stent and biomaterial covering of the present invention in an unwrapped condition and mounted on a dual release wire catheter;

Figure 2 is a side sectional view of the self-expanding stent and acellular matrix mounted on a single release wire catheter;

Figure 3 is a sectional view of the self-expanding stent of Figure 2 partially covered with an acellular matrix;

Figure 4 is a sectional view of the self-expanding stent of Figure 2 fully covered with an acellular matrix; and

Figure 5 is a perspective view of another self-expanding stent which can be incorporated into the present invention.

Figure 6 is a sectional view of another embodiment of the stent and biomaterial covering of the present invention mounted on a catheter.

Detailed Description of the Invention

A stent to be used with the present invention is illustrated in Figure 1. Stent 12 is more particularly described in United States Patent no. 5,342,387, the contents of which are incorporated herein by reference. In this embodiment, stent 12 is self-expanding. However, the present invention also contemplates utilizing any self-expandable or balloon expandable stent. Figures 1 and 6 are illustrations of self-expandable stents.

Referring to Figure 2, the stent 12 is illustrated mounted on a catheter 14. Acellular matrix 16 is mounted between the catheter 14 and the stent 12, presenting an inner lining for the stent 12.

Acellular matrix 16 of the preferred embodiments is derived from mammalian, preferably a human vessel, including blood vessels, namely arteries and veins, ducts, or conduits, and are therefore, tubular in shape having open ends. The size of the vessel to be harvested is dictated by the size and type of stent to be implanted in the patient. Preferably, acellular matrix 16 is extracted from human sources. However, bovine, porcine, canine or similar mammalian sources may also be suitable. Further, cryo-preserved human veins or other ducts or conduits are contemplated as being a suitable source for the biomaterial.

The method of extracting and preparing the matrix 16 is fully described in Courtman et al.: "Development of Pericardial Acellular Matrix Biomaterial: Biochemical and Mechanical Effects of Cell Extraction" Journal of Biomedical Materials Research, Vol. 28, 655-666 (1994), and Wilson et al. "Acellular Matrix Allograft Small Caliber Vascular Protheses", Vol. XXXVI Trans. AM. Soc. Artif. Intern Organs, (1990), and United States Patent nos. 4,776,853 and 4,801,299, all of which are incorporated herein by reference.

The acellular matrix material may be seeded by placing it in a high density culture medium of endothelial cells that are either from the host or some other mammalian source. The acellular matrix material may be seeded with endothelial cells before or after the acellular matrix is placed inside the stent by placing it in a high density culture medium. Alternatively, the seeding may be done *in situ*. Methods of endothelial seeding are known in the art. (Thompson et al.: "Effect of Seeding Time and Density on Endothelial Cell

Attachment to Damaged Vascular Surfaces" Br. J. Surg. 1993, Vol. 80). (Combe et al.: "Endothelial Seeding of Vascular Prosthesis: A Technique of In Situ Enzymatic Retrieval of Endothelial Cells without Vein Sacrifice" Annals of Vascular Surgery 1993, Vol. 7, No. 5).

The endothelial cells may be seeded in a monolayer or layers on the acellular matrix.

Stent 12 may have an internal protective sheath or sleeve 18. Sheath 18 has a longitudinally extending slot 20. Slot 20 allows access for distal end 22 and proximal end 24 of the stent to be inserted into notches 26 and 28 in the catheter 14. Notches 26 and 28 receive, respectively, the distal end 22 and proximal end 24 of stent 12 to retain the stent for deployment. Proximal end 24 is first engaged with the release wire 30 and then the distal end 22 is wound down to compact the stent 12. The distal end 22 is then looped through with the release wire 30. Release wire 30 extends internally within the catheter 14 through loops formed in each the distal end 22 and proximal end 24 of the stent 12 to retain the stent 12 on the catheter 14 in a compacted condition.

Once the stent 12 engages the release wire 30, the protective sheath or sleeve 18 can be withdrawn by sliding it along the catheter towards the proximal end thereof. After the protective sheath 18 is withdrawn, the distal end 32 of acellular matrix 16 is rolled back over itself to cover the distal end of stent 22. Similarly, the proximal end 34 is rolled over itself to cover the proximal end 24 of stent 12.

Referring to Figure 3, the distal end 32 is rolled back to cover only a portion of the distal end region of the stent 12. Similarly, the proximal end 34 is rolled back a portion of the length of stent 12 to cover the proximal end region thereof.

The distal end 32 and the proximal end 34 are attached to the inner tubular body of the acellular matrix 16 by suturing, surgical stapling, gluing, taping, or any other method for attaching biomaterial to itself.

The stent 12 and acellular matrix 16 can now be deployed using techniques and methods well known in the art.

Although the preferred embodiment has described the acellular matrix 16 being mounted on a catheter for covering the stent 12, it is now readily understood that similar cylindrical apparatus could be used. The stent 12 and acellular matrix 16 of the present invention could be mounted on such cylinder and later transferred to a stent for implantation.

Referring to Figure 4, the distal end 32 and the proximal end 34 of acellular matrix 16 are fully retracted until the ends 32 and 34 abut. A continuous suture line may be used around the circumferential seam for joining the ends 32 and 34 together. In this embodiment, the stent 12 is fully covered, both internally and externally and may be deployed using techniques and methods well known in the art.

It is noted that the distal end 22 and proximal end 24 of stent 12 extend through the acellular matrix 16 when in the ready for deployment condition. Once the release wire 30 is retracted, the distal end 22 and the proximal end 24 of stent 12 will retract back through the punctured opening in acellular matrix 16 which will close, fully covering stent 12.

The stent 12 and acellular matrix 16 are also useful in grafting. The stent 12 and acellular matrix 16 may be implanted on ends of a blood vessel which are to be joined. The stent 12 will provide improved structural support for the vessel over conventional prior art grafts. This improved support will reduce the risk of aneurysms.

Additionally, the stent 12 and acellular matrix 16 can be made of a larger diameter to operate as a graft for larger ducts within the human body. For example, the stent 12 and acellular matrix 16 of the present invention has applications as a prothesis for the trachea, oesophagus, alimentary canal, genitourinary or other similar bodily ducts.

Referring to Figure 5, a second embodiment of a self-expanding stent 112 which could be covered and implanted by the present invention is illustrated.

Referring to Figure 6, another embodiment of the present invention is illustrated. The acellular matrix 16 is attached to the stent 12 when stent 12 is in the expanded state. Stent 12 is then collapsed and mounted on the catheter 14. Guide wire 36 is inserted through catheter 14. A protective outer sheath 38 is then placed over said stent 12.

The acellular matrix 16 may be attached to stent 12 by suturing, surgical stapling, taping, gluing or by any other suitable method for attaching the biomaterial which would be apparent to a skilled person.

Additionally, the acellular matrix 16 may be seeded with mammalian endothelial cells, preferably human endothelial cells, before or after it is mounted on the catheter 14 or *in situ* once the stent 12 is delivered to the target site.

The stent 12 and acellular matrix 16 can now be deployed to the target site by removing the protective sheath 38 and expanding said stent 12.

The above embodiments are illustrations of the invention. It will be obvious to those skilled in the art that various modifications and changes can be made to these embodiments without departing from the spirit and scope of the invention.

We claim:

1. A method of preparing a stent for implantation, the method comprising the step of placing an open ended tube of biomaterial relatively inside the stent.

2. A method as claimed in claim 1 including a first preliminary step of coaxially mounting the tube onto a distal end of a catheter.

3. A method as claimed in claim 2 wherein said method comprises the further steps of attaching the biomaterial to said stent by suturing, surgical stapling, gluing or taping.

4. A method as claimed in claim 2 wherein said method comprises the further step of rolling open ends of the tube back over itself.

5. A method as claimed in claim 4 including after said rolling step, attaching said ends of the tube to itself.

6. A method as claimed in claim 5 wherein said attachment step includes suturing, surgical stapling, gluing, or taping.

7. A method as claimed in claim 1 wherein said implantation is for free grafting ends of a vessel in a patient.

8. A method as claimed in claim 1 wherein said biomaterial is seeded with endothelial cells.

9. A method as claimed in claim 8 wherein said endothelial cells are mammalian cells.

10. The use of a stent with biomaterial for treating occlusion and stenosis of a blood vessel comprising the steps of:

providing a catheter having a distal end;

mounting biomaterial on the distal end of said catheter;

sliding a stent over the biomaterial;

attaching said biomaterial to said stent by suturing, surgical stapling, gluing or taping said biomaterial to said stent;

delivering the stent and biomaterial to a target site;

expanding the stent; and

withdrawing said catheter.

11. The use of a stent with biomaterial as claimed in claim 10 wherein said use comprises the further step of placing a protective sheath over said stent after attaching said biomaterial to said stent whereby on delivering said stent and biomaterial to a target side, the outer sheath is removed from the stent and said stent is expanded.

12. The use of a stent with biomaterial as claimed in claim 10 wherein said biomaterial is an acellular matrix.

13. The use of a stent with biomaterial as claimed in claim 12 wherein said acellular matrix is derived from a vessel selected from a group comprising of human, bovine, canine, or porcine sources.

14. The use of a stent with biomaterial as claimed in claim 12 wherein said acellular matrix is derived from human bodily vessels.

15. The use of a stent with biomaterial as claimed in claim 12 wherein said acellular matrix is seeded with endothelial cells.

16. The use of a stent with biomaterial as claimed in claim 12 wherein said acellular matrix is seeded with endothelial cells after delivering the stent and acellular matrix to said target site.

17. The use of a stent with biomaterial for preventing occlusion and stenosis of a blood vessel comprising the steps of:

providing a catheter having a distal end and an internal release wire;

mounting a tubular acellular matrix on the distal end of said catheter;

sliding a self-expanding stent over the matrix, said self-expanding stent having a protective sheath;

extending distal and proximal ends of said stent to engage said release wire for contracting said stent into an implantable condition;

withdrawing said sheath;

rolling distal and proximal ends of said tubular acellular matrix over distal and proximal ends of said stent;

attaching said distal and proximal ends to said tubular acellular matrix;

inserting said catheter distal end into said blood vessel;

guiding said catheter distal end to a targeted portion of said blood vessel;

withdrawing said release wire allowing said self-expanding stent to expand; and

withdrawing said catheter from said blood vessel.

18. The use of a stent with biomaterial as claimed in claim 17 wherein said attachment step comprises attaching said distal and proximal ends of the tube together.

19. The use of a stent with biomaterial as claimed in claim 17 wherein said acellular matrix is derived from a vessel selected from a group comprising of human, bovine, canine, or porcine sources.

20. The use of a stent with biomaterial as claimed in claim 17 wherein said acellular matrix is derived from human bodily vessels.

21. The use of a stent with biomaterial as claimed in claim 17 wherein said acellular matrix is seeded with endothelial cells before inserting into the blood vessel.

22. The use of a stent with biomaterial as claimed in claim 17 wherein said acellular matrix is seeded with endothelial cells after inserting said catheter into the blood vessel.

23. A stent with a biomaterial covering.

24. A stent as claimed in claim 23 wherein said biomaterial is an acellular matrix.

25. A stent as claimed in claim 23 wherein said biomaterial is seeded with mammalian endothelial cells.

26. A stent as claimed in claim 24 wherein said acellular matrix is derived from a vessel selected from a group comprising of human, bovine, canine, porcine or other mammalian sources.

27. A stent as claimed in claim 24 wherein said acellular matrix is derived from human bodily vessels.

28. A stent as claimed in claim 24 wherein said acellular matrix is an inner tube with a distal and proximal end, said inner tube is inserted into said stent and said inner tube having open ends for rolling about ends of said stent and said distal and proximal ends are attached to said tube.

29. A stent as claimed in claim 28 wherein said acellular matrix is seeded with endothelial cells.

30. A stent as claimed in claim 24 wherein said acellular matrix is attached to said stent by suturing, surgical stapling, taping or gluing.

31. A stent as claimed in claim 30 wherein said stent and said acellular matrix is covered with a protective sheath.

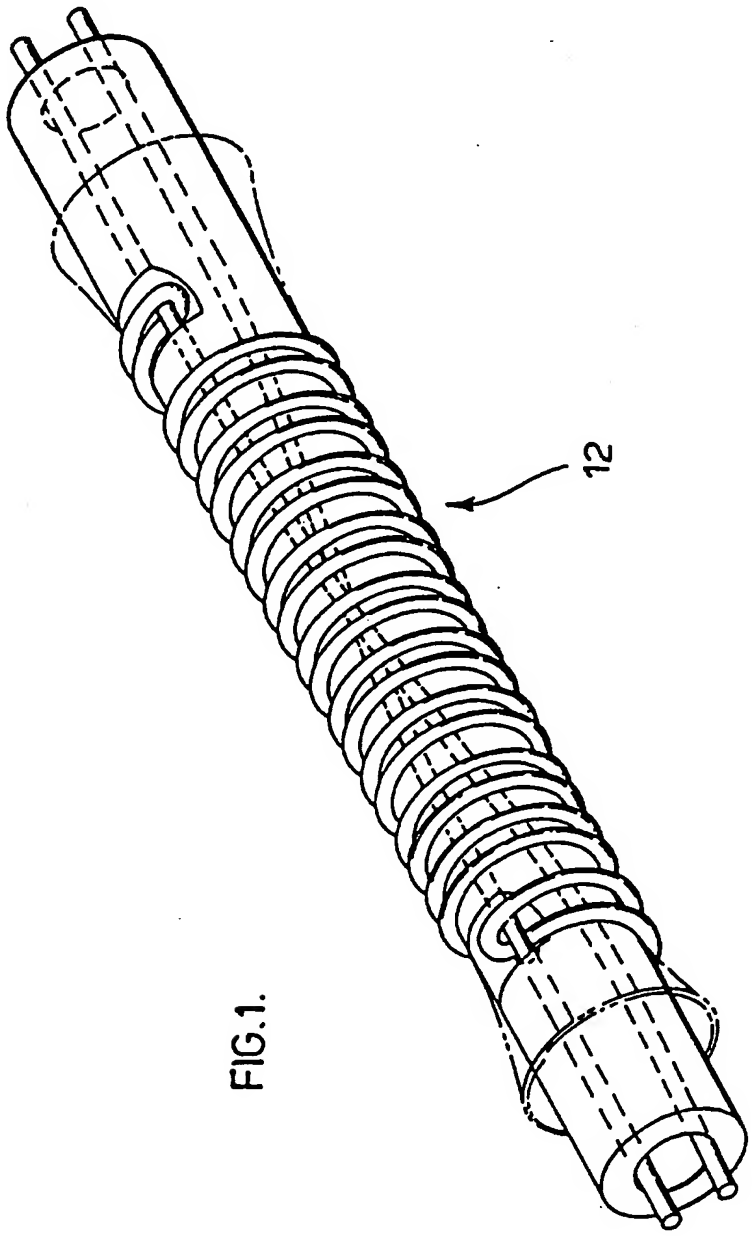

FIG.1.

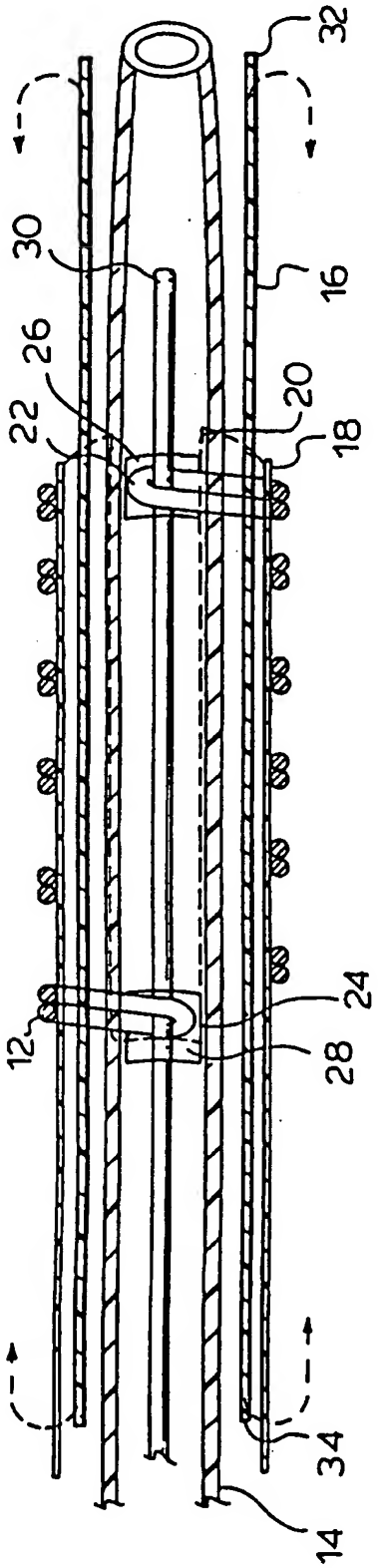

FIG.2.

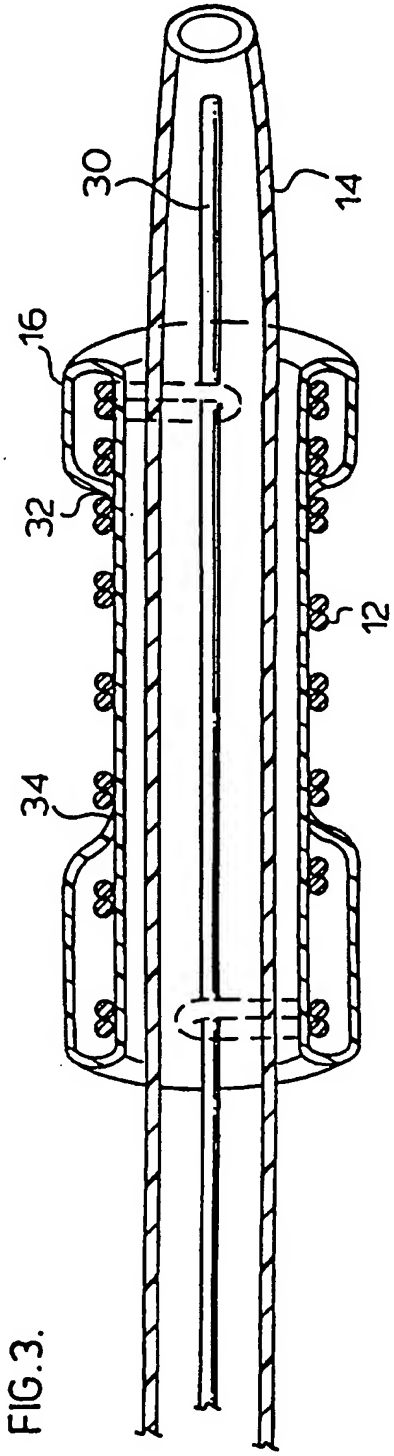

FIG.3.

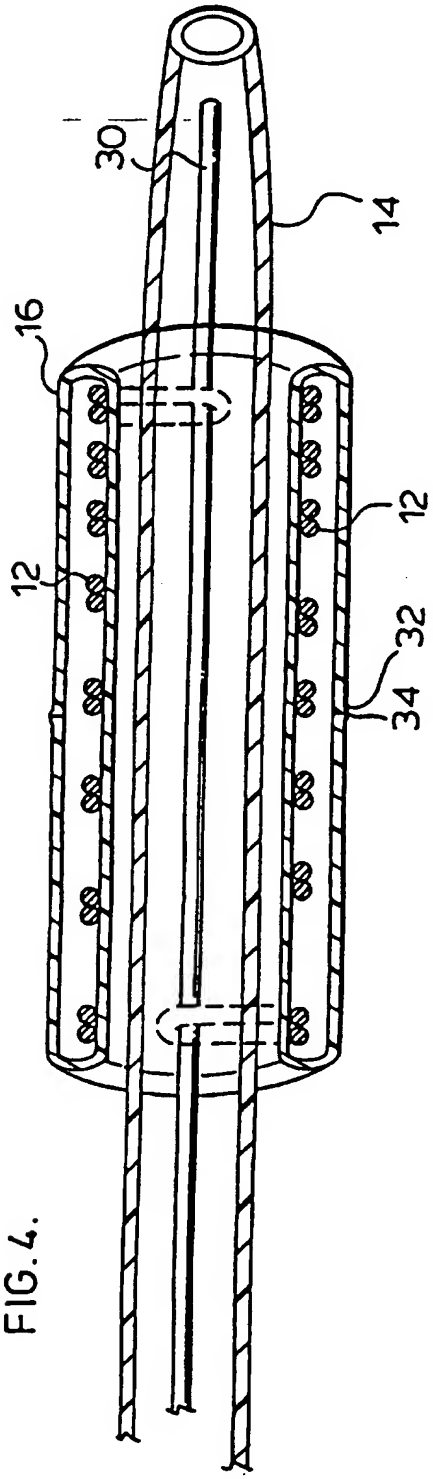

FIG.4.

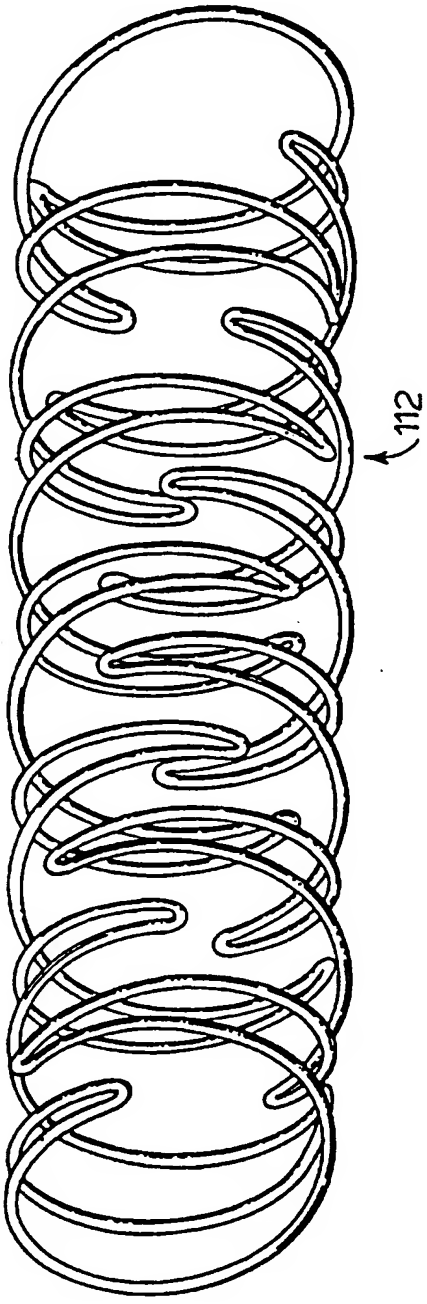

FIG.5.

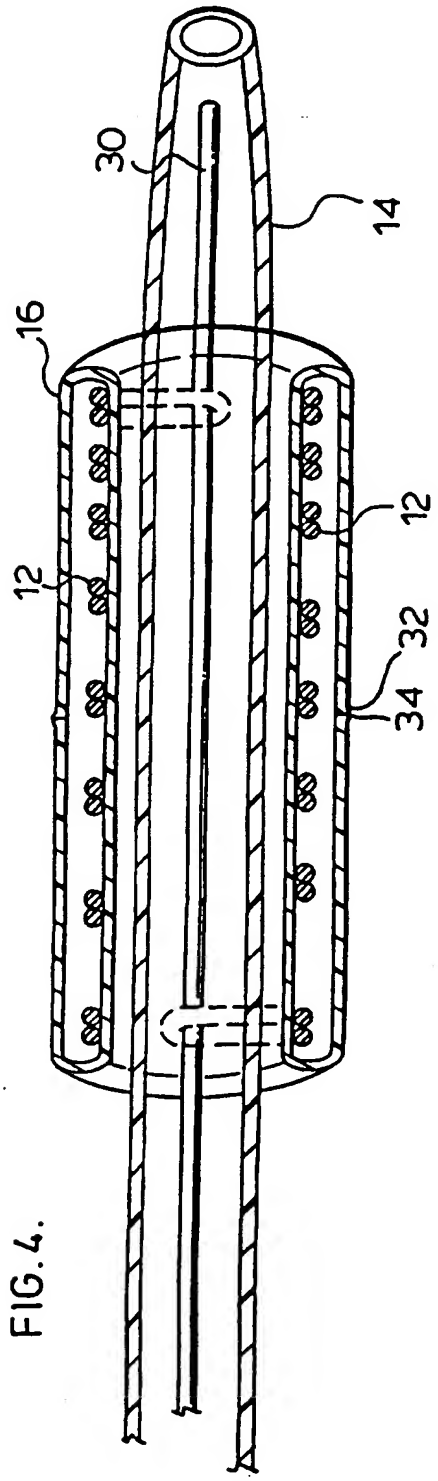

FIG.4.

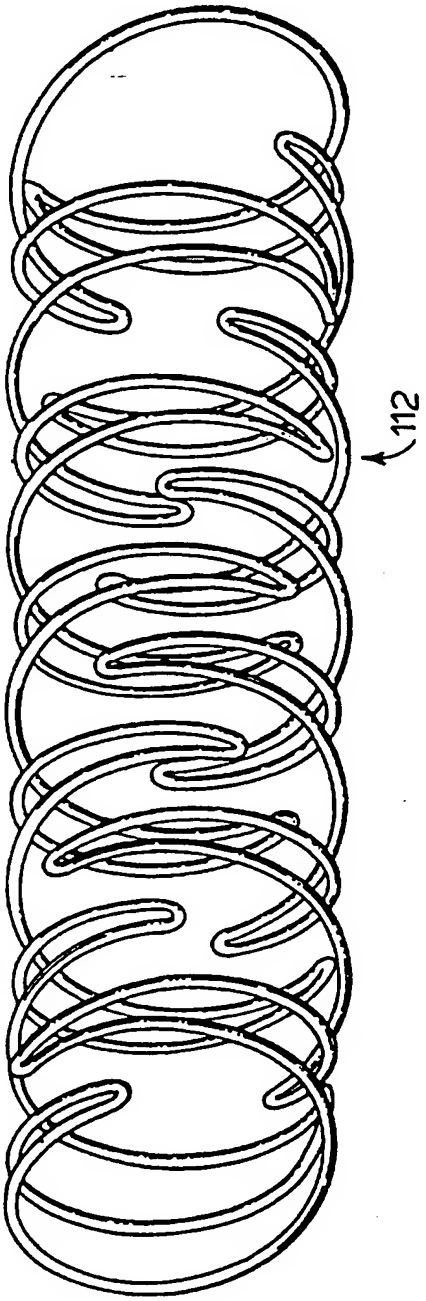

FIG.5.

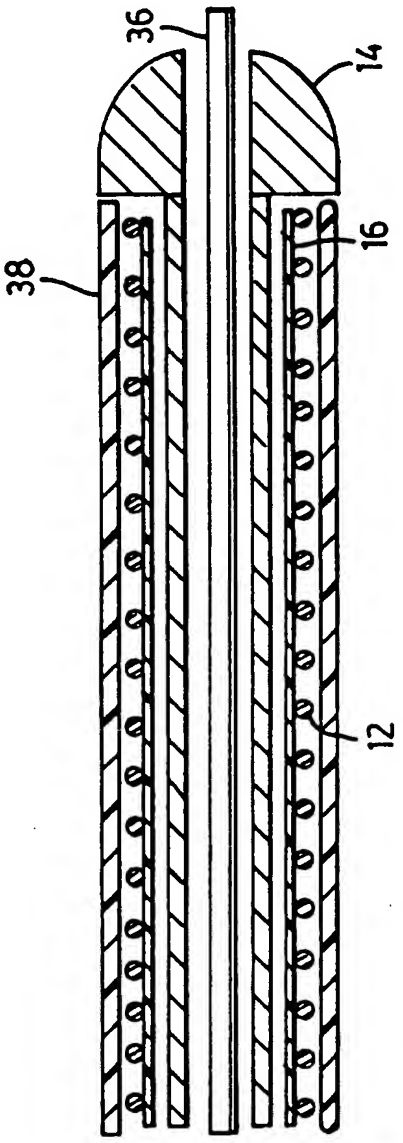

FIG.6

INTERNATIONAL SEARCH REPORT

Intern al Application No
PCT/CA 96/00663

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61F2/06 A61L27/00 A61L31/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61F A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 95 21592 A (MINTEC INC ;GOICOECHEA GEORGE (BS); HUDSON JOHN (US); MIALHE CLAUD) 17 August 1995 see page 19, line 24 - line 27; claims 32-35; figures see page 21, line 19 - line 24	1,7
P,X	WO 96 27347 A (GOVERNERS OF WAYNE STATE UNIVE ;TURI ZOLTAN G (US)) 12 September 1996 see page 6, line 4 - page 7, line 16; figures	1-7
P,X	WO 96 10375 A (CARDIOVASCULAR CONCEPTS INC ;KALMANN MENNO (NL); MOLL FRANCISCUS L) 11 April 1996 see page 9, line 1 - line 13; figures	1,2,4,7, 8
A		3,5

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[X] Further documents are listed in the continuation of box C.

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"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
5 February 1997	12. 02. 97

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl, Fax (+ 31-70) 340-3016	Neumann, E

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA 96/00663

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 10-31
because they relate to subject matter not required to be searched by this Authority, namely:
PCT Rule 39.1 (iv)

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searches without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Interr al Application No
PCT/CA 96/00663

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